42. (Twice amended) The peptide of claim 4 which is Cys-Leu-Asp-Pro-Lys-Gln-Lys-Trp-Ile-Gln (SEQ ID NO:7).

Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein, is respectfully requested. Claims 1 and 42 are amended. The amendments are made to further prosecution of the present application and are not intended to concede to the correctness of the Examiner's position or to prejudice the prosecution of claims present in a continuation application of the present application. Claims 1, 3-4, 6-11, and 42-43 are pending.

Amended claims 1 and 42 are supported by Example 2 in the specification. The amendment to claim 42 obviates the Examiner's objection to that claim at page 2 of the Office Action.

Upon a review of the marked and initialed Forms 1449 returned to Applicant's Representatives with the Office Action dated March 5, 2001, it was noted that Shibata et al. (Chem. Pharm. Bull., 43, 179 (1995)) was not marked as having been considered by the Examiner. A copy of the Form 1449 listing Shibata et al. accompanies this Amendment. Applicant respectfully requests that the Examiner mark and initial Shibata et al. as having been considered and return a copy of the marked and initialed Form 1449 with the next Official Communication.

The 35 U.S.C. § 102 Rejection

The Examiner rejected claims 1, 3-4 and 6-10 under 35 U.S.C. §102(b) as being anticipated by Yanofsky et al. (WO 95/20973). Yanofsky et al. do not disclose an isolated and purified peptide of a chemokine, a variant, or a derivative thereof, comprising no more than 30 amino acid residues, wherein the peptide comprises residues X_1-Asp-Pro-X_2-X_3-X_4-Trp-X_5-Gln or consists of X_2-X_3-X_4 or Trp-X_5-Gln, wherein X_1 is Ala or Leu, X_2 is Lys, Ser or Thr, X_4 is Lys, Glu, Ser or Arg, X_5 is Val or Ile, and X_3 is any amino acid, and wherein the peptide inhibits the activity of at least one native chemokine. Hence, withdrawal of the § 102(b) rejection of the claims is respectfully requested.

The 35 U.S.C. § 112, First Paragraph, Rejections

The Examiner rejected claims 1, 3-4, 6-11, and 42-43 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Examiner asserts that based on the unpredictability of the activity of a substituted protein, it would require undue experimentation by one of ordinary skill in the art to make and use the claimed invention. The Examiner also rejected claims 1, 3-4, 6-11, and 42-43 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These rejections, as they may be maintained with respect to the pending claims, are respectfully traversed.

As amended, the claims are directed to an isolated and purified peptide of a chemokine, a variant, or a derivative thereof, comprising no more than 30 amino acid residues, wherein the peptide comprises residues X_1-Asp-Pro-X_2-X_3-X_4-Trp-X_5-Gln or consists of X_2-X_3-X_4 or Trp-X_5-Gln, wherein X_1 is Ala or Leu, X_2 is Lys, Ser or Thr, X_4 is Lys, Glu, Ser or Arg, X_5 is Val or Ile and X_3 is any amino acid, and wherein the peptide inhibits the activity of at least one native chemokine.

To support the assertion that the activity of a substituted peptide is unpredictable, the Examiner cites Mikayama et al. (Proc. Natl. Acad. Sci. USA, 90, 10056 (1993)), Voet et al. (Biochemistry, John Wiley & Sons, Inc., pp. 126-128 and 228-234 (1990)) and Bowie et al. (Science, 247, 1306 (1990)). Mikayama et al. relate that murine glycosylation inhibiting factor (mGIF) had one amino acid substitution relative to human macrophage inhibitory factor (hMIF) but that recombinant mGIF had a different activity than recombinant hMIF (mGIF catalyzed the formation of unglycosylated IgE-binding factor from glycosylated IgE-binding factor but did not inhibit human macrophage migration while mMIF inhibited human macrophage migration but did not deglycosylate glycosylated IgE-binding factor). Voet et al. review the molecular bases for hemoglobinopathies, i.e., amino acid substitutions in globin. And although the Examiner alleges that Bowie et al. teaches that the position within a protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited, The

Examiner is requested to reconsider that Bowie states that "proteins are surprisingly tolerant of amino acid substitutions" (page 1406, column 2).

Regardless, all of the proteins in the references cited by the Examiner have at least 115 residues. Substitutions in those large proteins likely alter the structure and thus the activity of the protein. In contrast, the present claims are directed peptides of 30 residues or less. Moreover, none of these documents evidences that the recited amino acid substitutions in chemokine peptides have unpredictable effects on the function of the substituted peptide.

With respect to the predictability of the activity of the claimed variant chemokine peptides, the Examiner is respectfully requested to consider Applicant's specification. For example, page 106 shows ED_{50} data for four chemokines (MCP-1, MIP1α, IL8 and SDF-1α) and selected peptides, which include variants of a MCP-1 chemokine peptide. One of the variant peptides is designated $Leu_4Ser_7Ile_{11}$peptide3(1-12)[MCP-1] and has amino acid substitutions at positions 4, 7 and 11 relative to the sequence of a 12 amino acid peptide of human MCP-1 designated peptide 3(1-12)[MCP-1], another variant designated $Leu_4Ile_{11}Cys_{13}$ peptide3(1-12)MCP-1 has amino acid substitutions at positions 4, 11 and 13, and another variant, referred to as $Ser_7Glu_8Glu_9$peptide3(1-12)[MCP-1], has substitutions at positions 7, 8 and 9 relative to peptide 3(1-12)[MCP-1]. Other exemplary variant peptides of MCP-1 are Leu_4peptide3(1-12)[MCP-1], Ser_7peptide 3(1-12)[MCP-1], Ile_{11}peptide 3(1-12)[MCP-1], and Leu_4Ile_{11}peptide 3(1-12)[MCP-1] (see Table 5). The activities of these variants are shown in Table 6.

Thus, Applicant's specification demonstrates that substitutions in a MCP-1 derived peptide did not drastically alter the activity of those substituted peptides. Accordingly, Applicant's invention is enabled.

Further, as Applicant envisioned the detailed structure of the claimed chemokine peptides (see, for instance, Example 2 of the specification), Applicant, at the time the above-identified application was filed, was in possession of the claimed invention.

It is respectfully submitted that Applicant's specification fully complies with the requirements of § 112(1). Thus, withdrawal of the § 112(1) rejections of the claims is respectfully requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date September 5, 2001 By _____
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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 5 day of September, 2001.

Jane E. Brockschink
Name

_____
Signature